In this passage, Mercer and Birbeck tried to shift the discussion of artifacts to the more common sense in which an artifact is anything made by humans. The concern, however, as they make clear, is whether the micrograph can be interpreted so as to obtain good information about cell structure. That is, is the micrograph a reliable source of evidence or a *mere* artifact from which it is impossible to recover the structure of the cell with which the investigator began?

The concern with artifacts was widespread when cell fractionation and electron microscopy were first being introduced in the 1940s and 1950s. Writing at the close of the 1950s, at which point the techniques had acquired general acceptance, Alex Novikoff referred to a number of concerns about artifacts that had been prevalent:

> We can all recall the categorical assertion that hope for significant information concerning the *in vivo* function of subcellular particles was lost the moment the cell was disrupted or homogenized. Or, that the use of aqueous media like sucrose could yield only misleading particles, especially worthless nuclei. Or, that oxidative phosphorylation could never be retained once the organized structure of the complete mitochondrion was broken. Or, that electron microscopy was one huge blunder, based as it was on osmium artifacts. Or, that quantitative microspectrophotometry of stained tissue sections was deprived of meaning by the marked structural heterogeneity of the subcellular particles. Or, that enzyme destruction by fixative, and diffusion of reaction product during incubation, made staining methods worthless for demonstrating the intracellular *in situ* localization of enzymes, particularly important ones. (1959, p. 1)

By the time he was writing in 1959, though, Novikoff was putting all these worries in the past tense, referring to them as the "essentially destructive comments" by "gloomy critics" (p. 1). How in a relatively short time were these

examination are complicated and often brutal. They involve the treatment of the tissue with reagents which either violently precipitate proteins or slowly render them insoluble, followed by a series of solvents both aqueous and organic. The possibility of change is implicit in every step of this process, and it is the prime responsibility of the cytologist to inquire whether the structures which he displays in his preparation actually existed in the living cell, and if not, by what chemical process they have been produced. It is not surprising that during the history of this science, the results of investigation have been frequently challenged, sometimes on theoretical grounds based on biochemical experience, but often as the result of experiment. The list of structures which have been so challenged is a long one and includes most of the visible structures of the cell. To this list belong, among others, mitochondria, Nissl bodies of nerve cells, myofibrils of smooth and striated muscle, and the chromatin granules of the resting nuclei. All of these have been shown, by subsequent research, to be pre-existent in the living cell. On the other hand, artefacts have been produced by fixation. To this category belong the network of fibres described by the adherents of the reticular theory of the structure of the protoplasm, and the long filaments produced by Flemming in support of his filar theory" (1951, pp. 1–2).